BMJ open

Fear of childbirth predicts postpartum depression – a population-based analysis of 511,422 singleton births in Finland

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004047
Article Type:	Research
Date Submitted by the Author:	16-Sep-2013
Complete List of Authors:	Räisänen, Sari; Kuopio University Hospital, Obstetrics and Gynecology Lehto, Soili; University of Eastern Finland, Psychiatry Nielsen, Henriette; Copenhagen University Hospital, Fertility Clinic Gissler, M; THL National Institute for Health and Welfare, Information Kramer, Michael; Emory University, Epidemiology Heinonen, Seppo; University of Eastern Finland, Kuopio University Hospital
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Obstetrics and gynaecology, Mental health
Keywords:	EPIDEMIOLOGY, MENTAL HEALTH, Maternal medicine < OBSTETRICS, Depression & mood disorders < PSYCHIATRY, STATISTICS & RESEARCH METHODS

Fear of childbirth predicts postpartum depression – a population-based analysis of 511,422 singleton births in Finland

Sari Räisänen (Corresponding author)
Department of Epidemiology, Rollins School of Public Health, Emory University
1518 Clifton Road NE, Atlanta, Georgia, USA
Department of Obstetrics and Gynaecology, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
Email: shraisan@student.uef.fi, Tel: 358503378258, Fax**:** 35817172486

Soili M. Lehto
Department of Psychiatry, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
Email: soili.lehto@kuh.fi

Henriette Svarre Nielsen
Fertility Clinic, Rigshospitalet, Copenhagen University Hospital
Blegdamsvej 9, Dk-2100 Copenhagen Ø, Denmark
E-mail: henriette.svarre.nielsen@regionh.dk

Mika Gissler
National Institute for Health and Welfare (THL)
P.O. Box 30, Paciuksenkatu 21, FI-00271 Helsinki, Finland
Nordic School of Public Health, Gothenburg, Sweden
Email: mika.gissler@thl.fi

Michael R. Kramer
Department of Epidemiology, Rollins School of Public Health, Emory University
1518 Clifton Road NE, Atlanta, Georgia, USA
Email: mkram02@emory.edu

Seppo Heinonen
Department of Obstetrics and Gynaecology, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
Email: seppo.heinonen@kuh.fi

Keywords: Birth, Childbirth, Population Register, Postpartum Depression, Register, Socioeconomic

Status

Word count: 2,497

Abstract

Objectives: To study how reproductive risks and perinatal outcomes are associated with postpartum depression treated in specialized health care defined according to the International Classification of Diseases (ICD) -10 codes, separately among women with and without a history of depression.

Design: A retrospective population–based case-control study using

Setting: Data gathered from three national health registers for the years 2002–2010

Participants: All singleton births (*n*=511,422) in Finland

Primary outcome measures: Prevalence of and risk factors for postpartum depression

Results: In total, 0.3% (1,438 of 511,422) of women experienced postpartum depression, the prevalence being 0.1% (431 of 511,422) in women without and 5.3% (1,007 of 18,888) in women with a history of depression. After adjustment for possible covariates, a history of depression was found to be the strongest risk factor for postpartum depression. Other strong predisposing factors for postpartum depression were fear of childbirth, caesarean birth, nulliparity and major congenital anomaly. Specifically, among the 30% of women with postpartum depression but without a history of depression, postpartum depression was shown to be associated with fear of childbirth (aOR 2.71, 95% CI 1.98 to 3.71), caesarean birth (aOR 1.38, 95% CI 1.08 to 1.76), preterm birth (aOR 1.67, 95% CI 1.08 to 2.59) and major congenital anomaly (aOR 1.68, 95% CI 1.16 to 2.44), when compared to women with no postpartum depression and no history of depression.

Conclusions: A history of depression was found to be the most important predisposing factor of postpartum depression. Women without previous episodes of depression were at increased risk of postpartum depression if adverse events occurred during the course of pregnancy, especially if they showed fear of childbirth.

Article summary

Article focus

- To study what kind of antenatal and perinatal outcomes were associated with physician diagnosed postpartum depression defined according to the International Classification of Diseases (ICD) - 10 codes, especially in women with no history of previous depression episodes.

Key messages

- A history of previous depression episode was the strongest risk factor for postpartum depression but one third of all cases occurred in women with no previous depression episodes.

- Among women without a history of postpartum depression, the strongest risk factor for postpartum depression was fear of childbirth, but an increased prevalence of postpartum depression was also associated with nulliparity, smoking during pregnancy, caesarean birth, prior terminations, major congenital anomalies and preterm birth.

Strengths and limitations

- Strengths of this study were physician-diagnosed postpartum depression and the population-based data gathered from three mandatory national health registers.

- A possible limitation was that information on history of depression was based on outpatient and inpatient visits only since 1998 and 1996, respectively.

Introduction

Postpartum depression encompasses disorders ranging in severity from baby blues to postpartum psychosis (1) with onset of episodes within four to six weeks after birth (2). It has been suggested that about 50-80% of women suffer from baby blues after birth,(1) but estimates of the prevalence of postpartum depressive disorders vary substantially depending on assessment and timing of screening, sample size and population characteristics. Most previous studies have identified depressive symptoms by interviews or self-report depression screening instruments, such as the Edinburgh Postnatal Depression Scale (EPDS),(3) whereas studies based on doctor diagnoses are scarce. A systematic review by Gavin et al. suggested that approximately 20% of women suffer from minor or major depression during the first three months after the birth (4). Similarly, a systematic review by Gaynes et al. suggested that the prevalence of major depression ranges from 1.0% to 5.9%, while the prevalence of major and minor depression varies from 6.5% to 12.9% during the first postpartum year (5). However, the studies included in both systematic reviews primarily had small sample sizes, which were not population representative. This might have affected the reliability of the results, and therefore there is need for further studies with larger populations. A previous 20-year population-based study from the United States of America (USA) reported that only 0.06% and 0.26% of 2.4 million women were hospitalized with definite or possible postpartum depression, respectively, identified based on the International Classification of Diseases (ICD) in the USA (6).

The aetiology of postpartum depression is still unclear, but several predisposing risk factors may be important. According to Beck's meta-analysis, prenatal depression, low self esteem, childcare stress, prenatal anxiety, life stress, low social support, poor marital relationship, history of depression, infant temperament, maternity blues, single marital status, low socioeconomic status and unwanted pregnancy were associated with an increased risk of postpartum depression (7).

Women with adverse perinatal outcomes, such as caesarean (8) or preterm birth,(9) have also been shown to suffer more frequently from postpartum depression. Further, women with perinatal depression have been shown to suffer more frequently from diabetes mellitus and gestational diabetes (10,11).

The present study analyzed data on the deliveries of 511,422 women with singleton births in Finland for a 9 year period from 2002-2010. Information on history of depression was based on ICD-10 codes assigned during all inpatient visits since 1996 and hospital outpatient visits since 1998 gathered from the national Hospital Discharge Register. Information on postpartum depression was gathered until six weeks after birth. The aim of the present work was to investigate how reproductive risk factors and perinatal outcomes associate with postpartum depression defined according to ICD-10 codes. The specific aim was to study what kind of antenatal and perinatal exposures were associated with postpartum depression as an outcome, especially in women with no history of depression, because such information would be useful for prediction and counseling in clinics. Finland has around 5.5 million residents and a welfare system with mainly publicly funded health services.

Materials and Methods

Data and population

The sources of the data were three national health registers currently maintained by the National Institute for Health and Welfare; the Finnish Medical Birth Register (MBR), the Hospital Discharge Register (HDR) and the Congenital Malformations Register. The MBR was established in 1987 and contains demographic, pregnancy and delivery information on all live births or stillbirths delivered after the 22nd gestational week or weighing 500 g or more during the first postnatal week. The MBR data for 2002-2010 was supplemented by data on ICD-10 codes assigned for depression from

1996-2010 and fear of childbirth obtained from the HDR, which was established in 1969 and contains information on all aspects of inpatient care and outpatient visits in Finnish hospitals. The Congenital Malformations Register gathers information on major congenital anomalies (yes/no) until one year of age from several health registers, such as the MBR and HDR. The information gathered from the three registers was linked together using women's encrypted unique personal identification numbers. Data included all singleton births (*n*=511,422) in Finland from 2002-2010, whereas multiple births were excluded since they carry a higher risk of complications.

Authorization to use the data was obtained from the National Institute for Health and Welfare as required by the national data protection legislation law in Finland (Reference number 1749/5.05.00/2011).

Variables and definitions

Depression defined by ICD-10 codes F31.3, F31.5 and F32-34 was used to group women into four categories; 1) no postpartum depression and no history of depression, 2) no postpartum depression with a history of depression, 3) postpartum depression without a history of depression, and 4) postpartum depression with a history of depression. A history of depression was defined as any depression diagnosis between 1996 and delivery. Socioeconomic status (SES) categorization was based on international recommendations applied to Finland's National Classification of Occupations.(12) SES was grouped into five categories based on maternal occupation at birth: upper white-collar workers, e.g., physicians and teachers; lower white-collar workers, e.g., nurses and secretaries; blue-collar workers, e.g., cooks and cashiers; others; and missing information as published elsewhere (13). 'Others' included all unspecified occupations, such as entrepreneurs and students, retired, unemployed and housewives, while the category with missing SES information comprised 17.4% (*n*=89,041) of all the births. Self-reported smoking habits during an index pregnancy was grouped into three categories: non-smoking, quitted smoking during the first

trimester or continued smoking after the first trimester, i.e., smoking. Women with no prior births were classified as nulliparous and women with at least one previous birth were classified as multiparous. Fear of childbirth was defined according to the ICD-10 code O99.80 established in 1997. Marital status was classified as either married/living with a partner or single. Information on in vitro fertilization (IVF) included intracytoplasmic sperm injection and frozen embryo transfers. Information on prior miscarriages and terminations was dichotomous (yes or no). Body mass index (BMI) was defined as an individual's body mass divided by the square of their height from data available in the registries since 2004. Anemia was defined as hemoglobin levels ≤ 6.2 mmol/l during pregnancy. Stillbirth was defined as fetal death and early neonatal death as death during the first seven postnatal days. The gestational age was estimated based on the first- or second-trimester ultrasonography measurements. Preterm birth was defined as gestational age < 37+0 weeks. Small for gestational age (SGA) was defined as sex- and parity-specific birth weight more than two standard deviations (SDs) below the mean weight for gestation based on the current Finnish population-based reference.(14) Low birth weight (LBW) was defined as less than 2,500 grams. Five minute Apgar scores of <7 and infant's vein pH < 7.15 were considered low (this information was available in the registries from 2004).

Statistical analyses

Differences between groups of categorical variables were evaluated by chi-square test and continuous variables by the Kruskal-Wallis test. Risk factors for postpartum depression were determined by three multivariable logistic regression analyses: among the total population using women with no postpartum depression without or with a history of depression (categories 1 and 2) as a reference group, and subgroup analysis separately for women with postpartum depression with and without a history of depression using women with no postpartum depression and no history of depression (category 1) as a reference group. Candidate confounders and mediators were selected

based on bivariable analyses (p<0.1). Differences were deemed to be significant if p<0.05. In addition, 95% confidence intervals (CI) were calculated. The data were analyzed using SPSS for Windows 19.0, Chicago, IL.

Results

The prevalence of postpartum depression was 0.3% (1,438 of 511,422) among all women with singleton births: 0.1% (431 of 511,422) among women without and 5.3% (1,007 of 18,888) among women with a history of depression (Table 1). Women who experienced postpartum depression were more often nulliparous and smokers with single marital status and unspecified SES, and gave birth more frequently by cesarean section compared to women without postpartum depression (Tables 1). Furthermore, women experiencing postpartum depression were more likely to have reproductive risk factors, such as prior terminations, anemia, amniocentesis, gestational diabetes, maternal diabetes mellitus and fear of childbirth compared to women without postpartum depression (Table 1).

Table 2 shows the prevalence of perinatal outcomes according to postpartum depression and a history of depression. It appeared that women with postpartum depression more frequently had children born preterm and delivered by caesarean as well children with LBW, SGA, low 5 minute Apgar score and a major congenital anomaly, and had more admissions to a neonatal intensive care unit regardless of a history of depression compared to women without postpartum depression.

After adjustment for possible confounders, a history of depression was found to be the strongest risk factor for postpartum depression: depression during pregnancy was associated with a 140-fold (OR 139.6, 95% CI 120.6 to 161.6) and depression before pregnancy a three-fold (OR 3.14, 95% CI 2.71 to 3.63) greater odds of postpartum depression compared with women without a history of depression (Table 3). Other associated risk factors were nulliparity, caesarean birth, fear of

childbirth and a major congenital anomaly. An IVF achieved pregnancy was associated with a 47% (aOR 0.53, 95% CI 0.28 to 0.99) lower odds of postpartum depression.

Table 4 presents multivariable analyses of risk factors for postpartum depression, separately for women without and with a history of depression, using women with no postpartum depression and no history of depression as a reference group. An increased prevalence of postpartum depression among women without a history of depression was associated with nulliparity, smoking during pregnancy, caesarean birth, prior terminations, fear of childbirth, a major congenital anomaly, and preterm birth when compared to the reference group with no postpartum depression. The strongest risk factor was fear of childbirth, which was associated with a 2.7-fold (aOR 2.71, 95% CI 1.98 to 3.71) increased odds of postnatal depression. Among women with postpartum depression and a history of depression, the strongest risk factors were fear of childbirth, smoking, low or unspecified SES and single marital status when compared to the reference group with no postpartum depression and no history of depression. Increased prevalence of postpartum depression was also associated with an advanced maternal age, anemia, gestational diabetes, a major congenital anomaly and admission to neonatal intensive care unit. Correspondingly, an IVF achieved pregnancy was associated with a 93% lower prevalence of postpartum depression (aOR 0.07, 95% CI 0.01 to 0.49).

Discussion

In 2002-2010, among the total Finnish population of women delivering singleton births, 0.3% experienced major physician-diagnosed postpartum depression as indicated by ICD-10 codes assigned during any medical visit in the six weeks following delivery. This figure is consistent with a previous large population-based study from the USA, which reported that 0.1-0.3% of women were hospitalized due to postpartum depression as defined by ICD-codes (6). As expected, in the present study, two-thirds of all cases occurred in women with a history of depressive symptoms before or during pregnancy, but one-third of all cases were considered low risk with no depression

history, making it difficult for healthcare professionals to identify these patients. The main finding was that an eventful obstetric history, including preterm birth, major congenital anomaly and cesarean birth, and especially fear of childbirth were associated with postpartum depression in low risk women with no depression history before or during pregnancy. The fear of childbirth appeared to increase the prevalence of postpartum depression by about three-fold in women without a history of depression and five-fold in women with known depressive disease.

Strengths of this study include population-based detection of physician-diagnosed postpartum depression and the availability of data on a large number of possible additional risk factors contained in the three mandatory national health registers. The utilization of diagnoses to define postpartum depression lead to high specificity, whereas smaller studies based on self-reported screening by EDPS have reported a prevalence of 7.5-13.0% (15-17). A possible limitation was that information on prior history of depression was based on outpatient and inpatient visits only since 1998 and 1996, respectively. Additionally, SES could not be determined for 17.4% of the women, which may be explained by the age of the parturient, since a large proportion were students or housewives, and therefore more likely to stay at home to take care of children compared with older women. Further, due to concerns over confidentiality, a number of women did not provide that sensitive information.

The study showed that a history of depression before and/or during pregnancy was the most important risk factor for postpartum depression. A novel finding was that physician-diagnosed fear of childbirth was the strongest risk factor after previous history of depression and increased the prevalence of postpartum depression by around three- and five-fold among women without and with a previous history of depression, respectively. These results are consistent with a prior meta-analysis, which suggested that prenatal depression and maternal anxiety are risk factors for postpartum depression (7). Interestingly, women with a history of depression and an IVF achieved

pregnancy experienced substantially less postpartum depression. Other predisposing risk factors for postpartum depression among women with a previous history of depression were smoking, single marital status and low or unspecified SES, again was in line with the meta-analysis of Beck et al (7). This suggests that low self esteem, lack of social support, single marital status and low SES could be used as predictors of postpartum depression. Further, women with a history of depression and gestational diabetes experienced postpartum depression more frequently compared with women without depression, which was in line with several previous studies (10,11,18). This observation suggests that the pro-inflammatory state related to gestational diabetes may facilitate the development of postpartum depression (19). Correspondingly, pregnancies of women without a history of depression but with subsequent postpartum depression more frequently resulted in adverse perinatal outcomes, such as major congenital anomaly, preterm or caesarean birth, compared with women with no history of depression and no postpartum depression. Previous studies have also found an association between preterm birth, low birth weight, infant illness(9) and caesarean birth (8).

Based on this large, 9-year population-based study, we concluded that the burden of major physician-diagnosed postpartum depression, as defined by ICD-10 codes, is most frequent among women with a history of depression, but one third of all cases occur in low risk women with no prior history of depression. The challenge is to recognize this low risk group in a timely manner and identify the factors placing these apparently low risk women at high risk of developing postpartum depression. Adverse obstetric outcome has been known to lead to psychological distress, but this study demonstrates that fear of childbirth is also an important exposure and should be acknowledged by healthcare professionals.

The present study did not reveal whether giving birth was the ultimate trigger of depression in one third of women with no history of the disease or whether affected women would have been free of

depression for the rest of their lives if they had remained childless. Therefore, the long-term prognosis of postpartum depression recognized for the first time during pregnancy would be an interesting area of future research.

Ethical approval

Permission to use the confidential register data in this study was approved on 16th February, 2012 by the National Institute for Health and Welfare (THL) in Finland. (Reference number 1749/5.05.00/2011).

Acknowledgments: Sees-Editing Ltd for language editing.

Competing interests: None.

Funding: Study was supported by the Saastamoinen and the Emil Aaltonen foundations.

Data sharing: No additional data available.

Contributor statement

All authors participated in designing the study. SR managed the dataset and performed statistical analyses. SML, HSN, MG, MRK and SH were statistical advisors. All authors contributed to the interpretation of the results, as well as to writing and editing the manuscript.

References

1 Hubner-Liebermann B, Hausner H, Wittmann M. Recognizing and treating peripartum depression. Dtsch Arztebl Int 2012;109(24):419-24.

2 Wisner KL, Moses-Kolko EL, Sit DK. Postpartum depression: a disorder in search of a definition. Arch Womens Ment Health 2010;13(1):37-40.

3 Sit DK, Wisner KL. Identification of postpartum depression. Clin Obstet Gynecol 2009; 52(3):456-68.

4 Gavin NI, Gaynes BN, Lohr KN, et al. Perinatal depression: a systematic review of prevalence and incidence. Obstet Gynecol 2005;106(5 Pt 1):1071-83.

5 Gaynes BN, Gavin N, Meltzer-Brody S, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. Evid Rep Technol Assess (Summ) 2005; (119):1-8.

6 Savitz DA, Stein CR, Ye F, Kellerman L, et al. The epidemiology of hospitalized postpartum depression in New York State, 1995-2004. Ann Epidemiol 2011;21(6):399-406.

7 Beck CT. Predictors of postpartum depression: an update. Nurs Res 2001;50(5):275-85.

8 Barbadoro P, Cotichelli G, Chiatti C, et al. Socio-economic determinants and self-reported depressive symptoms during postpartum period. Women Health 2012;52(4):352-68.

9 Vigod SN, Villegas L, Dennis CL, et al. Prevalence and risk factors for postpartum depression among women with preterm and low-birth-weight infants: a systematic review. BJOG 2010; 117(5):540-50.

10 Bansil P, Kuklina EV, Meikle SF, et al. Maternal and fetal outcomes among women with depression. J Womens Health (Larchmt) 2010;19(2):329-34.

11 Kozhimannil KB, Pereira MA, Harlow BL. Association between diabetes and perinatal depression among low-income mothers. JAMA 2009;301(8):842-7.

12 Statistics Finland. Classification of Occupations 2001. http://www.stat.fi/meta/luokitukset/ammatti/001-2001/kuvaus_en.html (accessed 16th September 2013).

13 Gissler M, Rahkonen O, Arntzen A, et al. Trends in socioeconomic differences in Finnish perinatal health 1991-2006. J Epidemiol Community Health 2009;63(6):420-25.

14 Sankilampi U, Hannila ML, Saari A, et al. New population-based references for birth weight, length, and head circumference in singletons and twins from 23 to 43 gestation weeks. Ann Med 2013;45(5-6):446-54.

15 Tammentie T, Tarkka MT, Astedt-Kurki P, et al. Sociodemographic factors of families related to postnatal depressive symptoms of mothers. Int J Nurs Pract 2002;8(5):240-6.

16 Milgrom J, Gemmill AW, Bilszta JL, et al. Antenatal risk factors for postnatal depression: a large prospective study. J Affect Disord 2008;108(1-2):147-57.

17 Rubertsson C, Wickberg B, Gustavsson P, et al. Depressive symptoms in early pregnancy, two months and one year postpartum-prevalence and psychosocial risk factors in a national Swedish sample. Arch Womens Ment Health 2005;8(2):97-104.

18 Bowers K, Laughon SK, Kim S, et al. The Association between a Medical History of Depression and Gestational Diabetes in a Large Multi-ethnic Cohort in the United States. Paediatr Perinat Epidemiol 2013;27(4):323-8.

19 Osborne LM, Monk C. Perinatal depression-The fourth inflammatory morbidity of pregnancy?: Theory and literature review. Psychoneuroendocrinology 2013;38(10):1929–52.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
D **Title and abstract**	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **OK**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **OK**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **OK**
Objectives	3	State specific objectives, including any prespecified hypotheses **OK**
Methods		
Study design	4	Present key elements of study design early in the paper **OK**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **OK**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **OK**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed **NA**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **OK**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **OK**
Bias	9	Describe any efforts to address potential sources of bias **OK**
Study size	10	Explain how the study size was arrived at **TOTAL POPULATION**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **OK**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **OK**
		(*b*) Describe any methods used to examine subgroups and interactions **OK**
		(*c*) Explain how missing data were addressed **OK**
		(*d*) If applicable, explain how loss to follow-up was addressed **NO**
		(*e*) Describe any sensitivity analyses **OK**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **OK**
		(b) Give reasons for non-participation at each stage **NO**
		(c) Consider use of a flow diagram **NA**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **OK**
		(b) Indicate number of participants with missing data for each variable of interest **OK**
		(c) Summarise follow-up time (eg, average and total amount) **OK**
Outcome data	15*	Report numbers of outcome events or summary measures over time **OK**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included **OK**
		(*b*) Report category boundaries when continuous variables were categorized OK
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **OK**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **OK**
Discussion		
Key results	18	Summarise key results with reference to study objectives **OK**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **OK**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **OK**
Generalisability	21	Discuss the generalisability (external validity) of the study results **OK**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **OK**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Table 1. Delivery characteristics and reproductive risk factors among singleton births (*n*=511,422) in Finland from 2002-2010 according to postpartum depression and history of depression.

Mead (SD) or %	No postpartum depression, *n*=492,103 (96.2%)	No postpartum depression, *n*=17,881 (3.5%)	Postpartum depression, *n*= 431 (0.1%)	Postpartum depression, *n*=1,007 (0.2%)	*p value**
History of depression	No	Yes	No	Yes	
Nulliparous	42.0	45.5	52.2	49.0	≤0.001
Multiparous	58.0	54.5	47.8	51.0	
Mean maternal age , years (SD)	29.6 (5.4)	27.8 (6.1)	29.0 (5.9)	28.9 (5.9)	≤0.001
Mean gestational age, weeks (SD)	39.8 (1.8)	39.6 (1.9)	39.2 (2.7)	39.5 (2.0)	≤0.001
Mode of delivery %					
Vaginal spontaneous	75.8	74.4	66.2	69.2	≤0.001
Breech	0.6	0.5	0.7	0.2	
Forceps	0.1	0.1	0.0	0.0	
Vacuum assistance	7.7	7.5	8.2	7.8	
Caesarean section	15.9	17.5	24.9	22.9	
Mean birthweight, g (SD)	3531.5 (549)	3475.7 (551)	3388.7 (697)	3437.0 (599)	≤0.001
Male sex %	51.2	50.2	53.1	51.9	0.06
Induction %	16.6	19.8	17.4	21.7	≤0.001
Smoking status					≤0.001
Non-smoking	83.2	63.3	74.7	63.5	
Quit smoking during 1st trimester	3.7	7.0	5.1	7.1	
Smoking after 1st trimester	10.5	26.8	16.0	26.8	
Missing information	2.6	2.9	4.2	2.6	
Married or living with a partner	93.5	85.7	89.2	83.3	≤0.001
Socioeconomic status					≤0.001
Upper white-collar worker	8.6	3.7	6.7	4.4	
Lower white-collar worker	34.5	26.0	29.2	25.6	
Blue-collar worker	14.2	15.8	13.2	15.4	
Others [a]	25.7	31.1	28.8	29.9	
Missing information	17.2	23.4	22.0	24.7	
Mean prepregnancy BMI (SD) [b]	24.2 (4.7)	24.7 (5.3)	24.8 (5.3)	25.2 (5.7)	≤0.001
Prior miscarriages	20.7	23.6	17.9	22.3	≤0.001
Prior terminations	12.2	22.0	17.2	21.6	≤0.001
In vitro fertilization	1.6	1.3	2.3	0.1	≤0.001
Anemia (≤ 6.2 mmol/l)	1.6	2.7	1.6	2.9	≤0.001
Chorionic villus biopsy	1.0	1.3	0.7	1.1	0.05
Amniocentesis	2.5	2.3	4.2	3.0	0.03
Placenta praevia	0.3	0.3	0.7	0.3	0.36
Placental abruption	0.3	0.4	0.7	0.4	0.30
Preeclampsia	1.2	1.2	2.3	0.9	0.11
Gestational diabetes	11.2	13.8	17.4	17.6	≤0.001
Diabetes mellitus	8.4	11.1	14.6	13.3	≤0.001
Prior caesarean section	10.6	10.4	12.3	11.7	0.35
Fear of childbirth	4.6	12.0	11.8	19.1	≤0.001

SD=standard deviation, [a] 'Others' comprise entrepreneurs, students, retired women, unemployed women, housewives and all unclassifiable cases, [b] BMI= body mass index gathered since 2004, *Chi-square or Kruskal-Wallis test.

Table 2. Prevalence of perinatal outcomes among singleton births from 2002-2010 in Finland according to postpartum depression and history of depression.

	No postpartum depression, n/data available (%)	No postpartum depression, n/data available (%)	Postpartum depression, n/data available (%)	Postpartum depression, n/data available (%)	*p* value *
History of depression	No	Yes	No	Yes	
Admission to a neonatal intensive care unit	48,450/492,605 (9.8)	2,372/17,894 (13.3)	80/431 (18.6)	187/1,107(18.6)	≤0.001
Stillbirth	3,281/492,102 (0.7)	181/17,881 (1.0)	4/431 (0.9)	7/1,107 (0.7)	≤0.001
Early neonatal death	656/492,606 (0.1)	28/17,894 (0.2)	3/431(0.7)	2/1,107 (0.2)	0.01
Preterm birth (delivery weeks < 37)	22,052/491,089 (4.5)	1,045/17,826 (5.9)	51/535 (12.0)	65/1,004 (6.5)	≤0.001
Low birthweight (LBW) (< 2500 g)	16,109/492,095 (3.3)	763/17,871 (4.3)	40/429 (9.3)	51/1,006 (5.1)	≤0.001
Small for gestational age (SGA) (< -2SD)	18,162/490,771 (3.7)	814/17,815 (4.7)	27/422 (6.4)	54/1,004 (5.4)	≤0.001
Low Apgar score (< 7 at 5 min) [a]	6,970/326,860 (2.1)	384/13,275 (2.9)	14/299 (4.7)	46/770 (6.0)	≤0.001
Fetal venous pH < 7.15 at birth [b]	4,707/127,320 (3.7)	190/5,703 (3.3)	5/129 (3.9)	16/335 (4.8)	0.36
Major congenital anomaly	19,491/492,606 (4.0)	945/17,894 (5.3)	33/431 (7.7)	62/1,007 (7.7)	≤0.001
Cesarean section	78,091/492,606 (15.9)	3,133/17,894 (17.5)	107/431 (24.8)	230/1,007 (22.8)	≤0.001

[a] In registry since 2004, [b] determined by indication, in registry since 2004, *Chi-square test.

Table 3. Adjusted odds ratios (aOR) of postpartum depression (*n*=1,320) among women with singleton births from 2002-2010 in Finland, using women with no postpartum depression (without or with history of depression) as the comparison group (*n*=488,927).

Characteristic	Adjusted OR (95% CI)
Depression before pregnancy	3.14 (2.71-3.63)
Depression during pregnancy	139.60 (120.62-161.57)
Maternal age, years	
≤19	1
20–29	1.27 (0.96-1.68)
30–39	1.37 (1.02-1.84)
≥40	1.31 (0.87-1.96)
Nulliparous	1.24 (1.08-1.41)
Multiparous	1
Smoking status	
Non-smoking	1
Quit smoking during 1st trimester	1.07 (0.83-1.37)
Smoking after 1st trimester	1.10 (0.75-1.60)
Missing information	1.10 (0.75-1.60)
Married/living with a partner	1
Single	1.10 (0.92-1.32)
Socioeconomic status	
Upper white-collar worker	1
Lower white-collar worker	1.00 (0.75-1.32)
Blue-collar worker	1.04 (0.77-1.42)
Others [a]	1.16 (0.87-1.54)
Missing information	1.24 (0.92-1.65)
Mode of delivery	
Vaginal spontaneous	1
Breech	0.89 (0.35-2.30)
Forceps	NA
Vacuum assistance	1.09 (0.87-1.37)
Caesarean section	1.22 (1.05-1.42)
Prior miscarriages	0.92 (0.80-1.07)
Prior terminations	1.15 (0.98-1.35)
In vitro fertilization	0.53 (0.28-0.99)
Anemia (≤ 6.2 mmol/l)	1.08 (0.74-1.59)
Preeclampsia	0.92 (0.54-1.57)
Gestational diabetes	1.29 (0.99-1.68)
Maternal diabetes mellitus	1.04 (0.77-1.39)
Fear of childbirth	1.57 (1.32-1.87)
Major congenital anomaly	1.34 (1.05-1.72)
Admission to neonatal intensive care unit	1.17 (0.98-1.40)
Stillbirth	1.04 (0.54-2.02)
Low birthweight (<2500 g)	1.12 (0.80-1.56)
Preterm birth (≤37 weeks)	1.15 (0.86-1.54)
Male fetal sex	0.93 (0.83-1.05)

CI=Confidence Interval, NA= not applicable, [a] 'Others' comprise entrepreneurs, students, retired women, unemployed women, housewives and all unclassifiable cases.

Table 4. Adjusted odds ratios (OR) of postpartum depression among women with singleton births from 2002-2010 in Finland. The reference group was women with no postpartum depression and no history of depression (*n*=472,183) in both analyses.

	Postpartum depression without depression before and/or during pregnancy, *n*=400	Postpartum depression with depression before and/or during pregnancy, *n*=936
Characteristic	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Maternal age, years		
≤19	1	1.17 (0.87-1.57)
20–29	1.88 (0.95-3.75)	1
30–39	1.02 (0.59-1.75)	1.08 (0.94-1.24)
≥40	1.08 (0.63-1.83)	1.45 (1.08-1.95)
Nulliparous	1.42 (1.14-1.78)	1.34 (1.16-1.55)
Multiparous	1	1
Smoking status		
Non-smoking	1	1
Quit smoking during 1st trimester	1.34 (0.86-2.10)	2.12 (1.64-2.70)
Smoking after 1st trimester	1.43 (1.07-1.92)	2.62 (2.23-3.08)
Missing information	1.42 (0.81-2.48)	1.21 (0.79-1.86)
Married/living with a partner	1	1
Single	1.22 (0.87-1.72)	1.93 (1.61-2.31)
Socioeconomic status		
Upper white-collar worker	1	1
Lower white-collar worker	1.02 (0.67-1.54)	1.37 (0.98-1.93)
Blue-collar worker	0.95 (0.59-1.53)	1.63 (1.14-2.34)
Others [a]	1.38 (0.86-2.00)	2.01 (1.43-2.82)
Missing information	1.38 (0.90-2.§4)	2.39 (1.70-3.37)
Mode of delivery		
Vaginal spontaneous	1	1
Breech	1.28 (0.41-4.03)	0.40 (0.10-1.62)
Forceps	NA	NA
Vacuum assistance	1.18 (0.82-1.70)	0.99 (0.77-1.27)
Caesarean section	1.38 (1.08-1.76)	1.09 (0.92-1.29)
Prior miscarriages	0.90 (0.69-1.16)	1.11 (0.95-1.30)
Prior terminations	1.41 (1.08-1.84)	1.42 (1.20-1.67)
In vitro fertilization	1.40 (0.74-2.65)	0.07 (0.01-0.49)
Anemia (≤ 6.2 mmol/l)	1.02 (0.48-2.16)	1.66 (1.13-2.44)
Preeclampsia	1.31 (0.68-2.53)	0.65 (0.32-1.32)
Gestational diabetes	1.24 (0.78-1.96)	1.62 (1.23-2.14)
Maternal diabetes mellitus	1.59 (0.97-2.60)	1.03 (0.75-1.40)
Fear of childbirth	2.71 (1.98-3.71)	4.94 (4.17-5.86)
Major congenital anomaly	1.68 (1.16-2.44)	1.40 (1.08-1.83)
Admission to neonatal intensive care unit	1.29 (0.96-1.74)	1.76 (1.46-2.12)
Stillbirth	1.50 (0.56-4.06)	1.09 (0.68-1.45)
Low birthweight (<2500 g)	1.34 (0.82-2.20)	0.99 (0.68-1.45)
Preterm birth (≤37 weeks)	1.67 (1.08-2.59)	1.05(0.75-1.47)
Male fetal sex	0.94 (0.78-1.15)	0.96 (0.84-1.09)

CI=Confidence Interval, NA=not applicable, [a] 'Others' comprise entrepreneurs, students, retired women, unemployed women, housewives and all unclassifiable cases.

BMJ open

Fear of childbirth predicts postpartum depression – a population-based analysis of 511,422 singleton births in Finland

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004047.R1
Article Type:	Research
Date Submitted by the Author:	25-Oct-2013
Complete List of Authors:	Räisänen, Sari; Kuopio University Hospital, Obstetrics and Gynecology Lehto, Soili; University of Eastern Finland, Psychiatry Nielsen, Henriette; Copenhagen University Hospital, Fertility Clinic Gissler, M; THL National Institute for Health and Welfare, Information Kramer, Michael; Emory University, Epidemiology Heinonen, Seppo; University of Eastern Finland, Kuopio University Hospital
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Obstetrics and gynaecology, Mental health
Keywords:	EPIDEMIOLOGY, MENTAL HEALTH, Maternal medicine < OBSTETRICS, Depression & mood disorders < PSYCHIATRY, STATISTICS & RESEARCH METHODS

Fear of childbirth predicts postpartum depression – a population-based analysis of 511,422 singleton births in Finland

Sari Räisänen (Corresponding author)
Department of Epidemiology, Rollins School of Public Health, Emory University
1518 Clifton Road NE, Atlanta, Georgia, USA
Department of Obstetrics and Gynaecology, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
Email: shraisan@student.uef.fi, Tel: 358503378258, Fax**:** 35817172486

Soili M. Lehto
Department of Psychiatry, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
Email: soili.lehto@kuh.fi

Henriette Svarre Nielsen
Fertility Clinic, Rigshospitalet, Copenhagen University Hospital
Blegdamsvej 9, Dk-2100 Copenhagen Ø, Denmark
E-mail: henriette.svarre.nielsen@regionh.dk

Mika Gissler
National Institute for Health and Welfare (THL)
P.O. Box 30, Paciuksenkatu 21, FI-00271 Helsinki, Finland
Nordic School of Public Health, Gothenburg, Sweden
Email: mika.gissler@thl.fi

Michael R. Kramer
Department of Epidemiology, Rollins School of Public Health, Emory University
1518 Clifton Road NE, Atlanta, Georgia, USA
Email: mkram02@emory.edu

Seppo Heinonen
Department of Obstetrics and Gynaecology, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
Email: seppo.heinonen@kuh.fi

Keywords: Birth, Childbirth, Population Register, Postpartum Depression, Register, Socioeconomic

Status

Word count: 2917

Abstract

Objectives: To study how reproductive risks and perinatal outcomes are associated with postpartum depression treated in specialized health care defined according to the International Classification of Diseases (ICD) -10 codes, separately among women with and without a history of depression.

Design: A retrospective population–based case-control study using

Setting: Data gathered from three national health registers for the years 2002–2010

Participants: All singleton births (*n*=511,422) in Finland

Primary outcome measures: Prevalence of and risk factors for postpartum depression

Results: In total, 0.3% (1,438 of 511,422) of women experienced postpartum depression, the prevalence being 0.1% (431 of 511,422) in women without and 5.3% (1,007 of 18,888) in women with a history of depression. After adjustment for possible covariates, a history of depression was found to be the strongest risk factor for postpartum depression. Other strong predisposing factors for postpartum depression were fear of childbirth, caesarean birth, nulliparity and major congenital anomaly. Specifically, among the 30% of women with postpartum depression but without a history of depression, postpartum depression was shown to be associated with fear of childbirth (adjusted odds ratio (aOR) 2.71, 95% confidence interval (CI) 1.98 to 3.71), caesarean birth (aOR 1.38, 95% CI 1.08 to 1.77), preterm birth (aOR 1.65, 95% CI 1.08 to 2.56) and major congenital anomaly (aOR 1.67, 95% CI 1.15 to 2.42), when compared to women with no postpartum depression and no history of depression.

Conclusions: A history of depression was found to be the most important predisposing factor of postpartum depression. Women without previous episodes of depression were at increased risk of

postpartum depression if adverse events occurred during the course of pregnancy, especially if they showed physician-diagnosed fear of childbirth.

Article summary

Article focus

- To study what kind of antenatal and perinatal outcomes were associated with physician diagnosed postpartum depression defined according to the International Classification of Diseases (ICD) - 10 codes, especially in women with no history of previous depression episodes.

Key messages

- A history of previous depression episode was the strongest risk factor for postpartum depression but one third of all cases occurred in women with no previous depression episodes.

- Among women without a history of postpartum depression, the strongest risk factor for postpartum depression was physician-diagnosed fear of childbirth, but an increased prevalence of postpartum depression was also associated with nulliparity, smoking during pregnancy, caesarean birth, prior terminations, major congenital anomalies and preterm birth.

Strengths and limitations

- Strengths of this study were physician-diagnosed postpartum depression and the population-based data gathered from three mandatory national health registers.

- A possible limitation was that information on history of depression was based on outpatient and inpatient visits only since 1998 and 1996, respectively. We did not have information on cases diagnosed and treated in primary health care before year 2004.

Introduction

Postpartum depression encompasses disorders ranging in severity from baby blues to postpartum psychosis (1) with onset of episodes within four to six weeks after birth (2). It has been suggested that about 50-80% of women suffer from baby blues after birth,(1) but estimates of the prevalence of postpartum depressive disorders vary substantially depending on assessment and timing of screening, sample size and population characteristics. Most previous studies have identified depressive symptoms by interviews or self-report depression screening instruments, such as the Edinburgh Postnatal Depression Scale (EPDS),(3) whereas studies based on doctor diagnoses are scarce. A systematic review by Gavin et al. suggested that approximately 20% of women suffer from minor or major depression during the first three months after the birth (4). Similarly, a systematic review by Gaynes et al. suggested that the prevalence of major depression ranges from 1.0% to 5.9%, while the prevalence of major and minor depression varies from 6.5% to 12.9% during the first postpartum year (5). However, the studies included in both systematic reviews primarily had small sample sizes, which were not population representative. This might have affected the reliability of the results, and therefore there is need for further studies with larger populations. A previous 20-year population-based study from the United States of America (USA) reported that only 0.06% and 0.26% of 2.4 million women were hospitalized with definite or possible postpartum depression, respectively, identified based on the International Classification of Diseases (ICD) in the USA (6).

The aetiology of postpartum depression is still unclear, but several predisposing risk factors may be important. According to Beck's meta-analysis, prenatal depression, low self esteem, childcare stress, prenatal anxiety, life stress, low social support, poor marital relationship, history of depression, infant temperament, maternity blues, single marital status, low socioeconomic status and unwanted pregnancy were associated with an increased risk of postpartum depression (7).

Women with adverse perinatal outcomes, such as caesarean (8) or preterm birth,(9) have also been shown to suffer more frequently from postpartum depression. Further, women with perinatal depression have been shown to suffer more frequently from diabetes mellitus and gestational diabetes (10,11).

The present study analyzed data on the deliveries of 511,422 women with singleton births in Finland for a 9 year period from 2002-2010. Information on history of depression was based on ICD-10 codes assigned during all inpatient visits since 1996 and hospital outpatient visits since 1998 gathered from the national Hospital Discharge Register. Information on postpartum depression was gathered until six weeks after birth. The aim of the present work was to investigate how reproductive risk factors and perinatal outcomes associate with postpartum depression defined according to ICD-10 codes. The specific aim was to study what kind of antenatal and perinatal exposures were associated with postpartum depression as an outcome, especially in women with no history of depression, because such information would be useful for prediction and counseling in clinics. Finland has around 5.5 million residents and a welfare system with mainly publicly funded health services.

Materials and Methods

Data and population

The sources of the data were three national health registers currently maintained by the National Institute for Health and Welfare; the Finnish Medical Birth Register (MBR), the Hospital Discharge Register (HDR) and the Congenital Malformations Register. The MBR was established in 1987 and contains demographic, pregnancy and delivery information on all live births or stillbirths delivered after the 22nd gestational week or weighing 500 g or more during the first postnatal week. The MBR data for 2002-2010 was supplemented by data on ICD-10 codes assigned for depression from

1996-2010 and fear of childbirth obtained from the HDR, which was established in 1969 and contains information on all aspects of inpatient care and outpatient visits in Finnish hospitals. The Congenital Malformations Register gathers information on major congenital anomalies (yes/no) until one year of age from several health registers, such as the MBR and HDR. The information gathered from the three registers was linked together using women's encrypted unique personal identification numbers. Data included all singleton births (*n*=511,422) in Finland from 2002-2010, whereas multiple births were excluded since they carry a higher risk of complications.

Authorization to use the data was obtained from the National Institute for Health and Welfare as required by the national data protection legislation law in Finland (Reference number 1749/5.05.00/2011).

Variables and definitions

Depression defined by ICD-10 codes F31.3, F31.5 and F32-34 was used to group women into four categories; 1) no postpartum depression and no history of depression, 2) no postpartum depression with a history of depression, 3) postpartum depression without a history of depression, and 4) postpartum depression with a history of depression. A history of depression was defined as any depression diagnosis between 1996 and delivery. Information on depression was gathered until six weeks after birth. Depression was defined based on previous mentioned diagnoses and temporal association to pregnancy. Socioeconomic status (SES) categorization was based on international recommendations applied to Finland's National Classification of Occupations.(12) SES was grouped into five categories based on maternal occupation at birth: upper white-collar workers, e.g., physicians and teachers; lower white-collar workers, e.g., nurses and secretaries; blue-collar workers, e.g., cooks and cashiers; others; and missing information as published elsewhere (13). 'Others' included all unspecified occupations, such as entrepreneurs and students, retired, unemployed and housewives, while the category with missing SES information comprised 17.4%

(*n*=89,041) of all the births. Self-reported smoking during an index pregnancy was grouped into three categories: non-smoking, quitted smoking during the first trimester or continued smoking after the first trimester, i.e., smoking. Women with no prior births were classified as nulliparous and women with at least one previous birth were classified as multiparous. Fear of childbirth was defined according to the ICD-10 code O99.80 established in 1997. In Finland, feeling towards childbirth is asked for every woman during pregnancy in antenatal visits. Woman experiencing significant fear of childbirth who cannot be helped during antenatal visits in primary health care and/or having CS request due to fear of childbirth are referred to phobia clinics in maternity care. Physicians diagnose fear of childbirth if woman is referred for maternity care due to it or if fear of childbirth is manifested and dealt with during a visit in maternity care.{{1190 Saisto,T. 2013}} Marital status was classified as either married/living with a partner or single. Information on in vitro fertilization (IVF) included intracytoplasmic sperm injection and frozen embryo transfers. Information on prior miscarriages and terminations was dichotomous (yes or no). Body mass index (BMI) was defined as an individual's body mass divided by the square of their height from data available in the registries since 2004. Anemia was defined as hemoglobin levels ≤ 6.2 mmol/l during pregnancy. Stillbirth was defined as fetal death and early neonatal death as death during the first seven postnatal days. The gestational age was estimated based on the first- or second-trimester ultrasonography measurements. Preterm birth was defined as gestational age < 37+0 weeks. Small for gestational age (SGA) was defined as sex- and parity-specific birth weight more than two standard deviations (SDs) below the mean weight for gestation based on the current Finnish population-based reference.(14) Low birth weight (LBW) was defined as less than 2,500 grams. Five minute Apgar scores of <7 and infant's vein pH < 7.15 were considered low (this information was available in the registries from 2004).

Statistical analyses

Differences between groups of categorical variables were evaluated by chi-square test and continuous variables by the Kruskal-Wallis test. Risk factors for postpartum depression were determined by three multivariable logistic regression analyses: among the total population using women with no postpartum depression without or with a history of depression (categories 1 and 2) as a reference group, and subgroup analysis separately for women with postpartum depression with and without a history of depression using women with no postpartum depression and no history of depression (category 1) as a reference group. Candidate confounders and mediators were selected based on bivariable analyses (p<0.1). Differences were deemed to be significant if p<0.05. In addition, 95% confidence intervals (CI) were calculated. The data were analyzed using SPSS for Windows 19.0, Chicago, IL.

Results

The prevalence of postpartum depression was 0.3% (1,438 of 511,422) among all women with singleton births: 0.1% (431 of 511,422) among women without and 5.3% (1,007 of 18,888) among women with a history of depression (Table 1). Women who experienced postpartum depression were more often nulliparous and smokers with single marital status and unspecified SES, and gave birth more frequently by caesarean section compared to women without postpartum depression (Tables 1). Furthermore, women experiencing postpartum depression were more likely to have reproductive risk factors, such as prior terminations, anemia, amniocentesis, gestational diabetes, maternal diabetes mellitus and fear of childbirth compared to women without postpartum depression (Table 1).

Table 2 shows the prevalence of perinatal outcomes according to postpartum depression and a history of depression. It appeared that women with postpartum depression more frequently had children born preterm or stillbirth and delivered by caesarean as well children with LBW, SGA, low 5 minute Apgar score and a major congenital anomaly, and had more admissions to a neonatal

intensive care unit regardless of a history of depression compared to women without postpartum depression.

After adjustment for possible confounders, a history of depression was found to be the strongest risk factor for postpartum depression: depression during pregnancy was associated with a 140-fold (OR 139.35, 95% CI 120.40 to 161.28) and depression before pregnancy a three-fold (OR 3.14, 95% CI 2.72 to 3.64) greater odds of postpartum depression compared with women without a history of depression (Table 3). Other associated risk factors were nulliparity, caesarean birth, fear of childbirth and a major congenital anomaly. An IVF achieved pregnancy was associated with a 47% (aOR 0.53, 95% CI 0.28 to 0.99) lower odds of postpartum depression.

Table 4 presents multivariable analyses of risk factors for postpartum depression, separately for women without and with a history of depression, using women with no postpartum depression and no history of depression as a reference group. An increased prevalence of postpartum depression among women without a history of depression was associated with nulliparity, smoking during pregnancy, caesarean birth, prior terminations, fear of childbirth, a major congenital anomaly, and preterm birth when compared to the reference group with no postpartum depression. The strongest risk factor was fear of childbirth, which was associated with a 2.7-fold (aOR 2.71, 95% CI 1.98 to 3.71) increased odds of postnatal depression. Among women with postpartum depression and a history of depression, the strongest risk factors were fear of childbirth, stillbirth, smoking, low or unspecified SES and single marital status when compared to the reference group with no postpartum depression and no history of depression. Increased prevalence of postpartum depression was also associated with an advanced maternal age (≥40), anemia, prior terminations, gestational diabetes, a major congenital anomaly and admission to neonatal intensive care unit. Correspondingly, an IVF achieved pregnancy was associated with a 93% lower prevalence of postpartum depression (aOR 0.07, 95% CI 0.01 to 0.49).

Discussion

In 2002-2010, among the total Finnish population of women delivering singleton births, 0.3% experienced major physician-diagnosed postpartum depression as indicated by ICD-10 codes assigned during any medical visit in the six weeks following delivery. This figure is consistent with a previous large population-based study from the USA, which reported that 0.1-0.3% of women were hospitalized due to postpartum depression as defined by ICD-codes (6). As expected, in the present study, two-thirds of all cases occurred in women with a history of depressive symptoms before or during pregnancy, but one-third of all cases were considered low risk with no depression history, making it difficult for healthcare professionals to identify these patients. The novel and main finding of the present study was that an eventful obstetric history, including preterm birth, major congenital anomaly and caesarean birth, and especially physician-diagnosed fear of childbirth were associated with postpartum depression in low risk women with no depression history before or during pregnancy. The fear of childbirth appeared to increase the prevalence of postpartum depression by about three-fold in women without a history of depression and five-fold in women with known depressive disease.

Strengths of this study include population-based detection of physician-diagnosed postpartum depression and the availability of data on a large number of possible additional risk factors contained in the three mandatory national health registers. The utilization of diagnoses to define postpartum depression lead to high specificity, whereas smaller studies based on self-reported screening by EDPS have reported a prevalence of 7.5-13.0% (15-17). A possible limitation was that information on prior history of depression was based on outpatient and inpatient visits only since 1998 and 1996, respectively. Furthermore, we did not have complete information on cases diagnosed and treated in primary health care. Information on postpartum depression was gathered until six weeks after birth since it is defined as onset of episodes within four to six weeks after birth,

and thus women with later access to health care were not included. Additionally, SES could not be determined for 17.4% of the women, which may be explained by the age of the parturient, since a large proportion were students or housewives, and therefore more likely to stay at home to take care of children compared with older women. Further, due to concerns over confidentiality, a number of women did not provide that sensitive information.

The study showed that a history of depression before and/or during pregnancy was the most important risk factor for postpartum depression. A novel finding was that physician-diagnosed fear of childbirth was the strongest risk factor after previous history of depression and increased the prevalence of postpartum depression by around three- and five-fold among women without and with a previous history of depression, respectively. These results are consistent with a prior meta-analysis, which suggested that prenatal depression and maternal anxiety are risk factors for postpartum depression (7). Interestingly, women with a history of depression and an IVF achieved pregnancy experienced substantially less postpartum depression. Other predisposing risk factors for postpartum depression among women with a previous history of depression were smoking, single marital status and low or unspecified SES, again was in line with the meta-analysis of Beck et al (7). This suggests that low self-esteem, lack of social support, single marital status and low SES could be used as predictors of postpartum depression. Further, women with a history of depression and gestational diabetes experienced postpartum depression more frequently compared with women without depression, which was in line with several previous studies (10,11,18). This observation suggests that the pro-inflammatory state related to gestational diabetes may facilitate the development of postpartum depression (19). Correspondingly, pregnancies of women without a history of depression but with subsequent postpartum depression more frequently resulted in adverse perinatal outcomes, such as major congenital anomaly, preterm or caesarean birth, compared with women with no history of depression and no postpartum depression. Previous

studies have also found an association between preterm birth, low birth weight, infant illness (9) and caesarean birth (8).

Based on this large, 9-year population-based study, we concluded that the burden of major physician-diagnosed postpartum depression, as defined by ICD-10 codes, is most frequent among women with a history of depression, but one third of all cases occur in low risk women with no prior history of depression. The challenge is to recognize this low risk group in a timely manner and identify the factors placing these apparently low risk women at high risk of developing postpartum depression. Adverse obstetric outcome has been known to lead to psychological distress, but a novel finding of the present study was that physician-diagnose fear of childbirth is also an important exposure and should be acknowledged by healthcare professionals.

The present study did not reveal whether giving birth was the ultimate trigger of depression in one third of women with no history of the disease or whether affected women would have been free of depression for the rest of their lives if they had remained childless. Therefore, the long-term prognosis of postpartum depression recognized for the first time during pregnancy would be an interesting area of future research.

Ethical approval

Permission to use the confidential register data in this study was approved on 16th February, 2012 by the National Institute for Health and Welfare (THL) in Finland. (Reference number 1749/5.05.00/2011).

Acknowledgments: Sees-Editing Ltd for language editing.

Competing interests: None.

Funding: Study was supported by the Saastamoinen and the Emil Aaltonen foundations.

Data sharing: No additional data available.

Contributor statement

All authors participated in designing the study. SR managed the dataset and performed statistical analyses. SML, HSN, MG, MRK and SH were statistical advisors. All authors contributed to the interpretation of the results, as well as to writing and editing the manuscript.

References

1 Hubner-Liebermann B, Hausner H, Wittmann M. Recognizing and treating peripartum depression. Dtsch Arztebl Int 2012;109(24):419-24.

2 Wisner KL, Moses-Kolko EL, Sit DK. Postpartum depression: a disorder in search of a definition. Arch Womens Ment Health 2010;13(1):37-40.

3 Sit DK, Wisner KL. Identification of postpartum depression. Clin Obstet Gynecol 2009; 52(3):456-68.

4 Gavin NI, Gaynes BN, Lohr KN, et al. Perinatal depression: a systematic review of prevalence and incidence. Obstet Gynecol 2005;106(5 Pt 1):1071-83.

5 Gaynes BN, Gavin N, Meltzer-Brody S, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. Evid Rep Technol Assess (Summ) 2005; (119):1-8.

6 Savitz DA, Stein CR, Ye F, Kellerman L, et al. The epidemiology of hospitalized postpartum depression in New York State, 1995-2004. Ann Epidemiol 2011;21(6):399-406.

7 Beck CT. Predictors of postpartum depression: an update. Nurs Res 2001;50(5):275-85.

8 Barbadoro P, Cotichelli G, Chiatti C, et al. Socio-economic determinants and self-reported depressive symptoms during postpartum period. Women Health 2012;52(4):352-68.

9 Vigod SN, Villegas L, Dennis CL, et al. Prevalence and risk factors for postpartum depression among women with preterm and low-birth-weight infants: a systematic review. BJOG 2010; 117(5):540-50.

10 Bansil P, Kuklina EV, Meikle SF, et al. Maternal and fetal outcomes among women with depression. J Womens Health (Larchmt) 2010;19(2):329-34.

11 Kozhimannil KB, Pereira MA, Harlow BL. Association between diabetes and perinatal depression among low-income mothers. JAMA 2009;301(8):842-7.

12 Statistics Finland. Classification of Occupations 2001. http://www.stat.fi/meta/luokitukset/ammatti/001-2001/kuvaus_en.html (accessed 16th September 2013).

13 Gissler M, Rahkonen O, Arntzen A, et al. Trends in socioeconomic differences in Finnish perinatal health 1991-2006. J Epidemiol Community Health 2009;63(6):420-25.

14 Sankilampi U, Hannila ML, Saari A, et al. New population-based references for birth weight, length, and head circumference in singletons and twins from 23 to 43 gestation weeks. Ann Med 2013;45(5-6):446-54.

15 Tammentie T, Tarkka MT, Astedt-Kurki P, et al. Sociodemographic factors of families related to postnatal depressive symptoms of mothers. Int J Nurs Pract 2002;8(5):240-6.

16 Milgrom J, Gemmill AW, Bilszta JL, et al. Antenatal risk factors for postnatal depression: a large prospective study. J Affect Disord 2008;108(1-2):147-57.

17 Rubertsson C, Wickberg B, Gustavsson P, et al. Depressive symptoms in early pregnancy, two months and one year postpartum-prevalence and psychosocial risk factors in a national Swedish sample. Arch Womens Ment Health 2005;8(2):97-104.

18 Bowers K, Laughon SK, Kim S, et al. The Association between a Medical History of Depression and Gestational Diabetes in a Large Multi-ethnic Cohort in the United States. Paediatr Perinat Epidemiol 2013;27(4):323-8.

19 Osborne LM, Monk C. Perinatal depression-The fourth inflammatory morbidity of pregnancy?: Theory and literature review. Psychoneuroendocrinology 2013;38(10):1929–52.

Table 1. Delivery characteristics and reproductive risk factors among singleton births (*n*=511,422) in Finland from 2002-2010 according to postpartum depression and history of depression.

Mead (SD) or %	No postpartum depression, *n*=492,103 (96.2%)	No postpartum depression, *n*=17,881 (3.5%)	Postpartum depression, *n*= 431 (0.1%)	Postpartum depression, *n*=1,007 (0.2%)	*p value**
History of depression	No	Yes	No	Yes	
Nulliparous	42.0	45.5	52.2	49.0	≤0.001
Multiparous	58.0	54.5	47.8	51.0	
Mean maternal age , years (SD)	29.6 (5.4)	27.8 (6.1)	29.0 (5.9)	28.9 (5.9)	≤0.001
Mean gestational age, weeks (SD)	39.8 (1.8)	39.6 (1.9)	39.2 (2.7)	39.5 (2.0)	≤0.001
Mode of delivery %					
Vaginal spontaneous	75.8	74.4	66.2	69.2	≤0.001
Breech	0.6	0.5	0.7	0.2	
Forceps	0.1	0.1	0.0	0.0	
Vacuum assistance	7.7	7.5	8.2	7.8	
Caesarean section	15.9	17.5	24.9	22.9	
Mean birthweight, g (SD)	3531.5 (549)	3475.7 (551)	3388.7 (697)	3437.0 (599)	≤0.001
Male fetal sex %	51.2	50.2	53.1	51.9	0.06
Induction %	16.6	19.8	17.4	21.7	≤0.001
Smoking status					≤0.001
Non-smoking	83.2	63.3	74.7	63.5	
Quit smoking during 1st trimester	3.7	7.0	5.1	7.1	
Smoking after 1st trimester	10.5	26.8	16.0	26.8	
Missing information	2.6	2.9	4.2	2.6	
Married or living with a partner	93.5	85.7	89.2	83.3	≤0.001
Socioeconomic status					≤0.001
Upper white-collar worker	8.6	3.7	6.7	4.4	
Lower white-collar worker	34.5	26.0	29.2	25.6	
Blue-collar worker	14.2	15.8	13.2	15.4	
Others [a]	25.7	31.1	28.8	29.9	
Missing information	17.2	23.4	22.0	24.7	
Mean prepregnancy BMI (SD) [b]	24.2 (4.7)	24.7 (5.3)	24.8 (5.3)	25.2 (5.7)	≤0.001
Prior miscarriages	20.7	23.6	17.9	22.3	≤0.001
Prior terminations	12.2	22.0	17.2	21.6	≤0.001
In vitro fertilization	1.6	1.3	2.3	0.1	≤0.001
Anemia (≤ 6.2 mmol/l)	1.6	2.7	1.6	2.9	≤0.001
Chorionic villus biopsy	1.0	1.3	0.7	1.1	0.05
Amniocentesis	2.5	2.3	4.2	3.0	0.03
Placenta praevia	0.3	0.3	0.7	0.3	0.36
Placental abruption	0.3	0.4	0.7	0.4	0.30
Preeclampsia	1.2	1.2	2.3	0.9	0.11
Gestational diabetes	11.2	13.8	17.4	17.6	≤0.001
Diabetes mellitus	8.4	11.1	14.6	13.3	≤0.001
Prior caesarean section	10.6	10.4	12.3	11.7	0.35
Fear of childbirth	4.6	12.0	11.8	19.1	≤0.001

SD=standard deviation, [a] 'Others' comprise entrepreneurs, students, retired women, unemployed women, housewives and all unclassifiable cases, [b] BMI= body mass index gathered since 2004, *Chi-square or Kruskal-Wallis test.

Table 2. Prevalence of perinatal outcomes among singleton births from 2002-2010 in Finland according to postpartum depression and history of depression.

	No postpartum depression, n/data available (%)	No postpartum depression, n/data available (%)	Postpartum depression, n/data available (%)	Postpartum depression, n/data available (%)	*p* value *
History of depression	No	Yes	No	Yes	
Admission to a neonatal intensive care unit	48,450/492,605 (9.8)	2,372/17,894 (13.3)	80/431 (18.6)	187/1,007(18.6)	≤0.001
Stillbirth	1,514/492,606 (0.3)	67/17,894 (0.4)	5/431 (1.2)	8/1,007 (0.8)	≤0.001
Early neonatal death	656/492,606 (0.1)	28/17,894 (0.2)	3/431(0.7)	2/1,007 (0.2)	0.01
Preterm birth (delivery weeks < 37)	22,052/491,089 (4.5)	1,045/17,826 (5.9)	51/535 (12.0)	65/1,004 (6.5)	≤0.001
Low birthweight (LBW) (< 2500 g)	16,109/492,095 (3.3)	763/17,871 (4.3)	40/429 (9.3)	51/1,006 (5.1)	≤0.001
Small for gestational age (SGA) (< -2SD)	18,162/490,771 (3.7)	814/17,815 (4.7)	27/422 (6.4)	54/1,004 (5.4)	≤0.001
Low Apgar score (< 7 at 5 min) [a]	6,970/326,860 (2.1)	384/13,275 (2.9)	14/299 (4.7)	46/770 (6.0)	≤0.001
Fetal venous pH < 7.15 at birth [b]	4,707/127,320 (3.7)	190/5,703 (3.3)	5/129 (3.9)	16/335 (4.8)	0.36
Major congenital anomaly	19,491/492,606 (4.0)	945/17,894 (5.3)	33/431 (7.7)	62/1,007 (7.7)	≤0.001
Cesarean section	78,091/492,606 (15.9)	3,133/17,894 (17.5)	107/431 (24.8)	230/1,007 (22.8)	≤0.001

[a] In registry since 2004, [b] determined by indication, in registry since 2004, *Chi-square test.

Table 3. Adjusted odds ratios (aOR) of postpartum depression (*n*=1,320) among women with singleton births from 2002-2010 in Finland, using women with no postpartum depression (without or with history of depression) as the comparison group (*n*=490,287).

Characteristic	Adjusted OR (95% CI)
Depression before pregnancy	3.14 (2.72-3.64)
Depression during pregnancy	139.35 (120.40-161.28)
Maternal age, years	
≤19	1
20–29	1.27 (0.96-1.687)
30–39	1.37 (1.02-1.84)
≥40	1.30 (0.87-1.95)
Nulliparous	1.24 (1.08-1.41)
Multiparous	1
Smoking status	
Non-smoking	1
Quit smoking during 1st trimester	1.07 (0.83-1.37)
Smoking after 1st trimester	1.10 (0.75-1.60)
Missing information	1.09 (0.75-1.60)
Married/living with a partner	1
Single	1.10 (0.92-1.31)
Socioeconomic status	
Upper white-collar worker	1
Lower white-collar worker	1.00 (0.75-1.32)
Blue-collar worker	1.05 (0.77-1.42)
Others [a]	1.15 (0.87-1.53)
Missing information	1.23 (0.92-1.64)
Mode of delivery	
Vaginal spontaneous	1
Breech	0.83 (0.32-2.18)
Forceps	NA
Vacuum assistance	1.10 (0.87-1.37)
Caesarean section	1.23 (1.06-1.43)
Prior miscarriages	0.92 (0.80-1.07)
Prior terminations	1.15 (0.98-1.35)
In vitro fertilization	0.53 (0.28-0.99)
Anemia (≤ 6.2 mmol/l)	1.08 (0.74-1.59)
Preeclampsia	0.92 (0.54-1.58)
Gestational diabetes	1.29 (0.99-1.69)
Maternal diabetes mellitus	1.04 (0.77-1.39)
Fear of childbirth	1.58 (1.33-1.88)
Major congenital anomaly	1.33 (1.04-1.71)
Admission to neonatal intensive care unit	1.19 (1.00-1.43)
Stillbirth	2.00 (0.93-4.27)
Low birthweight (<2500 g)	1.12 (0.83-1.50)
Preterm birth (≤37 weeks)	0.81 (0.71-0.93)
Male fetal sex	1.07 (0.95-1.21)

CI=Confidence Interval, NA= not applicable, [a] 'Others' comprise entrepreneurs, students, retired women, unemployed women, housewives and all unclassifiable cases.

Table 4. Adjusted odds ratios (OR) of postpartum depression among women with singleton births from 2002-2010 in Finland. The reference group was women with no postpartum depression and no history of depression (*n*=472,183) in both analyses.

	Postpartum depression without depression before and/or during pregnancy, *n*=400	Postpartum depression with depression before and/or during pregnancy, *n*=936
Characteristic	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Maternal age, years		
≤19	1.88 (0.95-3.75)	1.20 (0.89-1.62)
20–29	1.02 (0.59-1.75)	1
30–39	1.08 (0.63-1.83)	1.04 (0.90-1.20)
≥40	1	1.37 (1.01-1.88)
Nulliparous	1.41 (1.13-1.76)	1.33 (1.15-1.54)
Multiparous	1	1
Smoking status		
Non-smoking	1	1
Quit smoking during 1st trimester	1.34 (0.86-2.10)	2.12 (1.64-2.70)
Smoking after 1st trimester	1.43 (1.07-1.92)	2.62 (2.23-3.08)
Missing information	1.41 (0.81-2.46)	1.19 (0.78-1.83)
Married/living with a partner	1	1
Single	1.22 (0.87-1.72)	1.93 (1.61-2.31)
Socioeconomic status		
Upper white-collar worker	1	1
Lower white-collar worker	1.02 (0.67-1.54)	1.37 (0.97-1.92)
Blue-collar worker	0.95 (0.59-1.53)	1.63 (1.14-2.34)
Others [a]	1.31 (0.86-2.00)	2.01 (1.43-2.82)
Missing information	1.38 (0.90-2.13)	2.38 (1.68-3.35)
Mode of delivery		
Vaginal spontaneous	1	1
Breech	1.25 (0.41-3.92)	0.38 (0.09-1.51)
Forceps	NA	NA
Vacuum assistance	1.19 (0.82-1.71)	0.99 (0.78-1.28)
Caesarean section	1.38 (1.08-1.77)	1.10 (0.93-1.30)
Prior miscarriages	0.90 (0.69-1.16)	1.11 (0.94-1.30)
Prior terminations	1.41 (1.08-1.84)	1.42 (1.21-1.67)
In vitro fertilization	1.40 (0.74-2.66)	0.07 (0.01-0.49)
Anemia (≤ 6.2 mmol/l)	1.02 (0.48-2.16)	1.66 (1.13-2.44)
Preeclampsia	1.32 (0.68-2.56)	0.67 (0.33-1.35)
Gestational diabetes	1.24 (0.78-1.96)	1.62 (1.23-2.14)
Maternal diabetes mellitus	1.59 (0.97-2.59)	1.03 (0.75-1.40)
Fear of childbirth	2.71 (1.98-3.71)	4.95 (4.18-5.87)
Major congenital anomaly	1.67 (1.15-2.42)	1.38 (1.06-1.81)
Admission to neonatal intensive care unit	1.32 (0.97-1.78)	1.81 (1.51-2.18)
Stillbirth	1.70 (0.52-5.60)	3.69 (1.77-7.69)
Low birthweight (<2500 g)	1.31 (0.80-2.16)	0.93 (0.63-1.36)
Preterm birth (≤37 weeks)	1.65 (1.08-2.56)	1.01 (0.72-1.41)
Male fetal sex	1.06 (0.87-1.29)	1.05 (0.92-1.19)

CI=Confidence Interval, NA=not applicable, [a] 'Others' comprise entrepreneurs, students, retired women, unemployed women, housewives and all unclassifiable cases.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
D **Title and abstract**	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **OK**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **OK**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **OK**
Objectives	3	State specific objectives, including any prespecified hypotheses **OK**
Methods		
Study design	4	Present key elements of study design early in the paper **OK**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **OK**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **OK**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed **NA**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **OK**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **OK**
Bias	9	Describe any efforts to address potential sources of bias **OK**
Study size	10	Explain how the study size was arrived at **TOTAL POPULATION**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **OK**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **OK**
		(*b*) Describe any methods used to examine subgroups and interactions **OK**
		(*c*) Explain how missing data were addressed **OK**
		(*d*) If applicable, explain how loss to follow-up was addressed **NO**
		(*e*) Describe any sensitivity analyses **OK**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **OK**
		(b) Give reasons for non-participation at each stage **NO**
		(c) Consider use of a flow diagram **NA**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **OK**
		(b) Indicate number of participants with missing data for each variable of interest **OK**
		(c) Summarise follow-up time (eg, average and total amount) **OK**
Outcome data	15*	Report numbers of outcome events or summary measures over time **OK**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included **OK**
		(*b*) Report category boundaries when continuous variables were categorized OK
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **OK**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **OK**
Discussion		
Key results	18	Summarise key results with reference to study objectives **OK**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **OK**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **OK**
Generalisability	21	Discuss the generalisability (external validity) of the study results **OK**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **OK**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Fear of childbirth predicts postpartum depression – a population-based analysis of 511,422 singleton births in Finland

Sari Räisänen (Corresponding author)
Department of Epidemiology, Rollins School of Public Health, Emory University
1518 Clifton Road NE, Atlanta, Georgia, USA
Department of Obstetrics and Gynaecology, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
Email: shraisan@student.uef.fi, Tel: 358503378258, Fax**:** 35817172486

Soili M. Lehto
Department of Psychiatry, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
Email: soili.lehto@kuh.fi

Henriette Svarre Nielsen
Fertility Clinic, Rigshospitalet, Copenhagen University Hospital
Blegdamsvej 9, Dk-2100 Copenhagen Ø, Denmark
E-mail: henriette.svarre.nielsen@regionh.dk

Mika Gissler
National Institute for Health and Welfare (THL)
P.O. Box 30, Paciuksenkatu 21, FI-00271 Helsinki, Finland
Nordic School of Public Health, Gothenburg, Sweden
Email: mika.gissler@thl.fi

Michael R. Kramer
Department of Epidemiology, Rollins School of Public Health, Emory University
1518 Clifton Road NE, Atlanta, Georgia, USA
Email: mkram02@emory.edu

Seppo Heinonen
Department of Obstetrics and Gynaecology, Kuopio University Hospital
P.O. Box 100, FI-70029 Kys, Kuopio, Finland
University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland
Email: seppo.heinonen@kuh.fi

Keywords: Birth, Childbirth, Population Register, Postpartum Depression, Register, Socioeconomic

Status

Word count: 2917

Abstract

Objectives: To study how reproductive risks and perinatal outcomes are associated with postpartum depression treated in specialized health care defined according to the International Classification of Diseases (ICD) -10 codes, separately among women with and without a history of depression.

Design: A retrospective population–based case-control study using

Setting: Data gathered from three national health registers for the years 2002–2010

Participants: All singleton births (*n*=511,422) in Finland

Primary outcome measures: Prevalence of and risk factors for postpartum depression

Results: In total, 0.3% (1,438 of 511,422) of women experienced postpartum depression, the prevalence being 0.1% (431 of 511,422) in women without and 5.3% (1,007 of 18,888) in women with a history of depression. After adjustment for possible covariates, a history of depression was found to be the strongest risk factor for postpartum depression. Other strong predisposing factors for postpartum depression were fear of childbirth, caesarean birth, nulliparity and major congenital anomaly. Specifically, among the 30% of women with postpartum depression but without a history of depression, postpartum depression was shown to be associated with fear of childbirth (adjusted odds ratio (aOR) 2.71, 95% confidence interval (CI) 1.98 to 3.71), caesarean birth (aOR 1.38, 95% CI 1.08 to 1.77), preterm birth (aOR 1.65, 95% CI 1.08 to 2.56) and major congenital anomaly (aOR 1.67, 95% CI 1.15 to 2.42), when compared to women with no postpartum depression and no history of depression.

Conclusions: A history of depression was found to be the most important predisposing factor of postpartum depression. Women without previous episodes of depression were at increased risk of

postpartum depression if adverse events occurred during the course of pregnancy, especially if they showed physician-diagnosed fear of childbirth.

Article summary

Article focus

- To study what kind of antenatal and perinatal outcomes were associated with physician diagnosed postpartum depression defined according to the International Classification of Diseases (ICD) - 10 codes, especially in women with no history of previous depression episodes.

Key messages

- A history of previous depression episode was the strongest risk factor for postpartum depression but one third of all cases occurred in women with no previous depression episodes.

- Among women without a history of postpartum depression, the strongest risk factor for postpartum depression was physician-diagnosed fear of childbirth, but an increased prevalence of postpartum depression was also associated with nulliparity, smoking during pregnancy, caesarean birth, prior terminations, major congenital anomalies and preterm birth.

Strengths and limitations

- Strengths of this study were physician-diagnosed postpartum depression and the population-based data gathered from three mandatory national health registers.

- A possible limitation was that information on history of depression was based on outpatient and inpatient visits only since 1998 and 1996, respectively. We did not have information on cases diagnosed and treated in primary health care before year 2004.

Introduction

Postpartum depression encompasses disorders ranging in severity from baby blues to postpartum psychosis (1) with onset of episodes within four to six weeks after birth (2). It has been suggested that about 50-80% of women suffer from baby blues after birth,(1) but estimates of the prevalence of postpartum depressive disorders vary substantially depending on assessment and timing of screening, sample size and population characteristics. Most previous studies have identified depressive symptoms by interviews or self-report depression screening instruments, such as the Edinburgh Postnatal Depression Scale (EPDS),(3) whereas studies based on doctor diagnoses are scarce. A systematic review by Gavin et al. suggested that approximately 20% of women suffer from minor or major depression during the first three months after the birth (4). Similarly, a systematic review by Gaynes et al. suggested that the prevalence of major depression ranges from 1.0% to 5.9%, while the prevalence of major and minor depression varies from 6.5% to 12.9% during the first postpartum year (5). However, the studies included in both systematic reviews primarily had small sample sizes, which were not population representative. This might have affected the reliability of the results, and therefore there is need for further studies with larger populations. A previous 20-year population-based study from the United States of America (USA) reported that only 0.06% and 0.26% of 2.4 million women were hospitalized with definite or possible postpartum depression, respectively, identified based on the International Classification of Diseases (ICD) in the USA (6).

The aetiology of postpartum depression is still unclear, but several predisposing risk factors may be important. According to Beck's meta-analysis, prenatal depression, low self esteem, childcare stress, prenatal anxiety, life stress, low social support, poor marital relationship, history of depression, infant temperament, maternity blues, single marital status, low socioeconomic status and unwanted pregnancy were associated with an increased risk of postpartum depression (7).

Women with adverse perinatal outcomes, such as caesarean (8) or preterm birth,(9) have also been shown to suffer more frequently from postpartum depression. Further, women with perinatal depression have been shown to suffer more frequently from diabetes mellitus and gestational diabetes (10,11).

The present study analyzed data on the deliveries of 511,422 women with singleton births in Finland for a 9 year period from 2002-2010. Information on history of depression was based on ICD-10 codes assigned during all inpatient visits since 1996 and hospital outpatient visits since 1998 gathered from the national Hospital Discharge Register. Information on postpartum depression was gathered until six weeks after birth. The aim of the present work was to investigate how reproductive risk factors and perinatal outcomes associate with postpartum depression defined according to ICD-10 codes. The specific aim was to study what kind of antenatal and perinatal exposures were associated with postpartum depression as an outcome, especially in women with no history of depression, because such information would be useful for prediction and counseling in clinics. Finland has around 5.5 million residents and a welfare system with mainly publicly funded health services.

Materials and Methods

Data and population

The sources of the data were three national health registers currently maintained by the National Institute for Health and Welfare; the Finnish Medical Birth Register (MBR), the Hospital Discharge Register (HDR) and the Congenital Malformations Register. The MBR was established in 1987 and contains demographic, pregnancy and delivery information on all live births or stillbirths delivered after the 22nd gestational week or weighing 500 g or more during the first postnatal week. The MBR data for 2002-2010 was supplemented by data on ICD-10 codes assigned for depression from

1996-2010 and fear of childbirth obtained from the HDR, which was established in 1969 and contains information on all aspects of inpatient care and outpatient visits in Finnish hospitals. The Congenital Malformations Register gathers information on major congenital anomalies (yes/no) until one year of age from several health registers, such as the MBR and HDR. The information gathered from the three registers was linked together using women's encrypted unique personal identification numbers. Data included all singleton births (*n*=511,422) in Finland from 2002-2010, whereas multiple births were excluded since they carry a higher risk of complications.

Authorization to use the data was obtained from the National Institute for Health and Welfare as required by the national data protection legislation law in Finland (Reference number 1749/5.05.00/2011).

Variables and definitions

Depression defined by ICD-10 codes F31.3, F31.5 and F32-34 was used to group women into four categories; 1) no postpartum depression and no history of depression, 2) no postpartum depression with a history of depression, 3) postpartum depression without a history of depression, and 4) postpartum depression with a history of depression. A history of depression was defined as any depression diagnosis between 1996 and delivery. Information on depression was gathered until six weeks after birth. Depression was defined based on previous mentioned diagnoses and temporal association to pregnancy. Socioeconomic status (SES) categorization was based on international recommendations applied to Finland's National Classification of Occupations.(12) SES was grouped into five categories based on maternal occupation at birth: upper white-collar workers, e.g., physicians and teachers; lower white-collar workers, e.g., nurses and secretaries; blue-collar workers, e.g., cooks and cashiers; others; and missing information as published elsewhere (13). 'Others' included all unspecified occupations, such as entrepreneurs and students, retired, unemployed and housewives, while the category with missing SES information comprised 17.4%

(*n*=89,041) of all the births. Self-reported smoking during an index pregnancy was grouped into three categories: non-smoking, quitted smoking during the first trimester or continued smoking after the first trimester, i.e., smoking. Women with no prior births were classified as nulliparous and women with at least one previous birth were classified as multiparous. Fear of childbirth was defined according to the ICD-10 code O99.80 established in 1997. In Finland, feeling towards childbirth is asked for every woman during pregnancy in antenatal visits. Woman experiencing significant fear of childbirth who cannot be helped during antenatal visits in primary health care and/or having CS request due to fear of childbirth are referred to phobia clinics in maternity care. Physicians diagnose fear of childbirth if woman is referred for maternity care due to it or if fear of childbirth is manifested and dealt with during a visit in maternity care.{{1190 Saisto,T. 2013}} Marital status was classified as either married/living with a partner or single. Information on in vitro fertilization (IVF) included intracytoplasmic sperm injection and frozen embryo transfers. Information on prior miscarriages and terminations was dichotomous (yes or no). Body mass index (BMI) was defined as an individual's body mass divided by the square of their height from data available in the registries since 2004. Anemia was defined as hemoglobin levels ≤ 6.2 mmol/l during pregnancy. Stillbirth was defined as fetal death and early neonatal death as death during the first seven postnatal days. The gestational age was estimated based on the first- or second-trimester ultrasonography measurements. Preterm birth was defined as gestational age < 37+0 weeks. Small for gestational age (SGA) was defined as sex- and parity-specific birth weight more than two standard deviations (SDs) below the mean weight for gestation based on the current Finnish population-based reference.(14) Low birth weight (LBW) was defined as less than 2,500 grams. Five minute Apgar scores of <7 and infant's vein pH < 7.15 were considered low (this information was available in the registries from 2004).

Statistical analyses

Differences between groups of categorical variables were evaluated by chi-square test and continuous variables by the Kruskal-Wallis test. Risk factors for postpartum depression were determined by three multivariable logistic regression analyses: among the total population using women with no postpartum depression without or with a history of depression (categories 1 and 2) as a reference group, and subgroup analysis separately for women with postpartum depression with and without a history of depression using women with no postpartum depression and no history of depression (category 1) as a reference group. Candidate confounders and mediators were selected based on bivariable analyses ($p<0.1$). Differences were deemed to be significant if $p<0.05$. In addition, 95% confidence intervals (CI) were calculated. The data were analyzed using SPSS for Windows 19.0, Chicago, IL.

Results

The prevalence of postpartum depression was 0.3% (1,438 of 511,422) among all women with singleton births: 0.1% (431 of 511,422) among women without and 5.3% (1,007 of 18,888) among women with a history of depression (Table 1). Women who experienced postpartum depression were more often nulliparous and smokers with single marital status and unspecified SES, and gave birth more frequently by caesarean section compared to women without postpartum depression (Tables 1). Furthermore, women experiencing postpartum depression were more likely to have reproductive risk factors, such as prior terminations, anemia, amniocentesis, gestational diabetes, maternal diabetes mellitus and fear of childbirth compared to women without postpartum depression (Table 1).

Table 2 shows the prevalence of perinatal outcomes according to postpartum depression and a history of depression. It appeared that women with postpartum depression more frequently had children born preterm or stillbirth and delivered by caesarean as well children with LBW, SGA, low 5 minute Apgar score and a major congenital anomaly, and had more admissions to a neonatal

intensive care unit regardless of a history of depression compared to women without postpartum depression.

After adjustment for possible confounders, a history of depression was found to be the strongest risk factor for postpartum depression: depression during pregnancy was associated with a 140-fold (OR 139.35, 95% CI 120.40 to 161.28) and depression before pregnancy a three-fold (OR 3.14, 95% CI 2.72 to 3.64) greater odds of postpartum depression compared with women without a history of depression (Table 3). Other associated risk factors were nulliparity, caesarean birth, fear of childbirth and a major congenital anomaly. An IVF achieved pregnancy was associated with a 47% (aOR 0.53, 95% CI 0.28 to 0.99) lower odds of postpartum depression.

Table 4 presents multivariable analyses of risk factors for postpartum depression, separately for women without and with a history of depression, using women with no postpartum depression and no history of depression as a reference group. An increased prevalence of postpartum depression among women without a history of depression was associated with nulliparity, smoking during pregnancy, caesarean birth, prior terminations, fear of childbirth, a major congenital anomaly, and preterm birth when compared to the reference group with no postpartum depression. The strongest risk factor was fear of childbirth, which was associated with a 2.7-fold (aOR 2.71, 95% CI 1.98 to 3.71) increased odds of postnatal depression. Among women with postpartum depression and a history of depression, the strongest risk factors were fear of childbirth, stillbirth, smoking, low or unspecified SES and single marital status when compared to the reference group with no postpartum depression and no history of depression. Increased prevalence of postpartum depression was also associated with an advanced maternal age (≥40), anemia, prior terminations, gestational diabetes, a major congenital anomaly and admission to neonatal intensive care unit. Correspondingly, an IVF achieved pregnancy was associated with a 93% lower prevalence of postpartum depression (aOR 0.07, 95% CI 0.01 to 0.49).

Discussion

In 2002-2010, among the total Finnish population of women delivering singleton births, 0.3% experienced major physician-diagnosed postpartum depression as indicated by ICD-10 codes assigned during any medical visit in the six weeks following delivery. This figure is consistent with a previous large population-based study from the USA, which reported that 0.1-0.3% of women were hospitalized due to postpartum depression as defined by ICD-codes (6). As expected, in the present study, two-thirds of all cases occurred in women with a history of depressive symptoms before or during pregnancy, but one-third of all cases were considered low risk with no depression history, making it difficult for healthcare professionals to identify these patients. The novel and main finding of the present study was that an eventful obstetric history, including preterm birth, major congenital anomaly and caesarean birth, and especially physician-diagnosed fear of childbirth were associated with postpartum depression in low risk women with no depression history before or during pregnancy. The fear of childbirth appeared to increase the prevalence of postpartum depression by about three-fold in women without a history of depression and five-fold in women with known depressive disease.

Strengths of this study include population-based detection of physician-diagnosed postpartum depression and the availability of data on a large number of possible additional risk factors contained in the three mandatory national health registers. The utilization of diagnoses to define postpartum depression lead to high specificity, whereas smaller studies based on self-reported screening by EDPS have reported a prevalence of 7.5-13.0% (15-17). A possible limitation was that information on prior history of depression was based on outpatient and inpatient visits only since 1998 and 1996, respectively. Furthermore, we did not have complete information on cases diagnosed and treated in primary health care. Information on postpartum depression was gathered until six weeks after birth since it is defined as onset of episodes within four to six weeks after birth,

and thus women with later access to health care were not included. Additionally, SES could not be determined for 17.4% of the women, which may be explained by the age of the parturient, since a large proportion were students or housewives, and therefore more likely to stay at home to take care of children compared with older women. Further, due to concerns over confidentiality, a number of women did not provide that sensitive information.

The study showed that a history of depression before and/or during pregnancy was the most important risk factor for postpartum depression. A novel finding was that physician-diagnosed fear of childbirth was the strongest risk factor after previous history of depression and increased the prevalence of postpartum depression by around three- and five-fold among women without and with a previous history of depression, respectively. These results are consistent with a prior meta-analysis, which suggested that prenatal depression and maternal anxiety are risk factors for postpartum depression (7). Interestingly, women with a history of depression and an IVF achieved pregnancy experienced substantially less postpartum depression. Other predisposing risk factors for postpartum depression among women with a previous history of depression were smoking, single marital status and low or unspecified SES, again was in line with the meta-analysis of Beck et al (7). This suggests that low self-esteem, lack of social support, single marital status and low SES could be used as predictors of postpartum depression. Further, women with a history of depression and gestational diabetes experienced postpartum depression more frequently compared with women without depression, which was in line with several previous studies (10,11,18). This observation suggests that the pro-inflammatory state related to gestational diabetes may facilitate the development of postpartum depression (19). Correspondingly, pregnancies of women without a history of depression but with subsequent postpartum depression more frequently resulted in adverse perinatal outcomes, such as major congenital anomaly, preterm or caesarean birth, compared with women with no history of depression and no postpartum depression. Previous

studies have also found an association between preterm birth, low birth weight, infant illness (9) and caesarean birth (8).

Based on this large, 9-year population-based study, we concluded that the burden of major physician-diagnosed postpartum depression, as defined by ICD-10 codes, is most frequent among women with a history of depression, but one third of all cases occur in low risk women with no prior history of depression. The challenge is to recognize this low risk group in a timely manner and identify the factors placing these apparently low risk women at high risk of developing postpartum depression. Adverse obstetric outcome has been known to lead to psychological distress, but a novel finding of the present study was that physician-diagnose fear of childbirth is also an important exposure and should be acknowledged by healthcare professionals.

The present study did not reveal whether giving birth was the ultimate trigger of depression in one third of women with no history of the disease or whether affected women would have been free of depression for the rest of their lives if they had remained childless. Therefore, the long-term prognosis of postpartum depression recognized for the first time during pregnancy would be an interesting area of future research.

Ethical approval

Permission to use the confidential register data in this study was approved on 16th February, 2012 by the National Institute for Health and Welfare (THL) in Finland. (Reference number 1749/5.05.00/2011).

Acknowledgments: Sees-Editing Ltd for language editing.

Competing interests: None.

Funding: Study was supported by the Saastamoinen and the Emil Aaltonen foundations.

Data sharing: No additional data available.

Contributor statement

All authors participated in designing the study. SR managed the dataset and performed statistical analyses. SML, HSN, MG, MRK and SH were statistical advisors. All authors contributed to the interpretation of the results, as well as to writing and editing the manuscript.

References

1 Hubner-Liebermann B, Hausner H, Wittmann M. Recognizing and treating peripartum depression. Dtsch Arztebl Int 2012;109(24):419-24.

2 Wisner KL, Moses-Kolko EL, Sit DK. Postpartum depression: a disorder in search of a definition. Arch Womens Ment Health 2010;13(1):37-40.

3 Sit DK, Wisner KL. Identification of postpartum depression. Clin Obstet Gynecol 2009; 52(3):456-68.

4 Gavin NI, Gaynes BN, Lohr KN, et al. Perinatal depression: a systematic review of prevalence and incidence. Obstet Gynecol 2005;106(5 Pt 1):1071-83.

5 Gaynes BN, Gavin N, Meltzer-Brody S, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. Evid Rep Technol Assess (Summ) 2005; (119):1-8.

6 Savitz DA, Stein CR, Ye F, Kellerman L, et al. The epidemiology of hospitalized postpartum depression in New York State, 1995-2004. Ann Epidemiol 2011;21(6):399-406.

7 Beck CT. Predictors of postpartum depression: an update. Nurs Res 2001;50(5):275-85.

8 Barbadoro P, Cotichelli G, Chiatti C, et al. Socio-economic determinants and self-reported depressive symptoms during postpartum period. Women Health 2012;52(4):352-68.

9 Vigod SN, Villegas L, Dennis CL, et al. Prevalence and risk factors for postpartum depression among women with preterm and low-birth-weight infants: a systematic review. BJOG 2010; 117(5):540-50.

10 Bansil P, Kuklina EV, Meikle SF, et al. Maternal and fetal outcomes among women with depression. J Womens Health (Larchmt) 2010;19(2):329-34.

11 Kozhimannil KB, Pereira MA, Harlow BL. Association between diabetes and perinatal depression among low-income mothers. JAMA 2009;301(8):842-7.

12 Statistics Finland. Classification of Occupations 2001. http://www.stat.fi/meta/luokitukset/ammatti/001-2001/kuvaus_en.html (accessed 16th September 2013).

13 Gissler M, Rahkonen O, Arntzen A, et al. Trends in socioeconomic differences in Finnish perinatal health 1991-2006. J Epidemiol Community Health 2009;63(6):420-25.

14 Sankilampi U, Hannila ML, Saari A, et al. New population-based references for birth weight, length, and head circumference in singletons and twins from 23 to 43 gestation weeks. Ann Med 2013;45(5-6):446-54.

15 Tammentie T, Tarkka MT, Astedt-Kurki P, et al. Sociodemographic factors of families related to postnatal depressive symptoms of mothers. Int J Nurs Pract 2002;8(5):240-6.

16 Milgrom J, Gemmill AW, Bilszta JL, et al. Antenatal risk factors for postnatal depression: a large prospective study. J Affect Disord 2008;108(1-2):147-57.

17 Rubertsson C, Wickberg B, Gustavsson P, et al. Depressive symptoms in early pregnancy, two months and one year postpartum-prevalence and psychosocial risk factors in a national Swedish sample. Arch Womens Ment Health 2005;8(2):97-104.

18 Bowers K, Laughon SK, Kim S, et al. The Association between a Medical History of Depression and Gestational Diabetes in a Large Multi-ethnic Cohort in the United States. Paediatr Perinat Epidemiol 2013;27(4):323-8.

19 Osborne LM, Monk C. Perinatal depression-The fourth inflammatory morbidity of pregnancy?: Theory and literature review. Psychoneuroendocrinology 2013;38(10):1929–52.